



## SEQUENCE LISTING

<110> Anderson, John P.  
Basi, Gurigbal  
Doane, Minh Tam  
Frigon, Normand  
John, Varghese  
Power, Michael  
Sinha, Sukanto  
Tatsuno, Gwen  
Tung, Jay  
Wang, Shuwen  
McConlogue, Lisa

<120> Beta-Secretase Enzyme Compositions and  
Methods

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<140> US 09/724,571

<141> 2000-11-28

<150> US 09/501,708

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10/20/2020

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<212> PRT
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<210> 51
<211> 5
<212> PRT
<213> Homo sapiens

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<400> 51
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<210> 52
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<212> PRT
<213> Artificial Sequence

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<220>
<223> Synthetic oligopeptide substrate

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<213> Artificial Sequence

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<220>
<223> Synthetic oligopeptide substrate

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Lys Thr Glu Glu Ile Ser Glu Val Asn Leu Asp Ala Glu Phe  
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<210> 56  
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 <212> PRT  
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<400> 56  
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 <212> PRT  
 <213> Homo sapiens

<400> 57  
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 Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp  
 35 40 45  
 Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val  
 50 55 60  
 Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr  
 65 70 75 80  
 Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser  
 85 90 95  
 Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr  
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 Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro  
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 Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln  
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 Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg  
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 Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala  
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 Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu  
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 Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala  
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 Val Ser Ala

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 <213> Homo sapiens

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 Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp  
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 Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu  
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 His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg  
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 Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu  
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 Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg  
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 Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly  
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 Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg  
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<212> PRT
<213> Homo sapiens
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Ser	Asn	Phe	Ala	Val	Gly	Ala	Ala	Pro	His	Pro	Phe	Leu	His	Arg	Tyr	
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Tyr	Val	Pro	Tyr	Thr	Gln	Gly	Lys	Trp	Glu	Gly	Glu	Leu	Gly	Thr	Asp	
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 195 200 205  
 Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln  
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 275 280 285  
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 Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp  
 305 310 315 320  
 Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr  
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 340 345 350  
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 355 360 365  
 Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala  
 370 375 380  
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 385 390 395 400  
 Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala  
 405 410 415  
 Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu  
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 Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro  
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 Gln Thr Asp Glu  
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<210> 60  
 <211> 420  
 <212> PRT  
 <213> Homo sapiens

<400> 60  
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 35 40 45  
 Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val  
 50 55 60  
 Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr  
 65 70 75 80  
 Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser  
 85 90 95  
 Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr  
 100 105 110  
 Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val  
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Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile		
145	150	155
Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp		160
	165	170
Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp		175
	180	185
Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro		190
	195	200
Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln		205
	210	215
Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile		220
225	230	235
Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg		240
	245	250
Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln		255
	260	265
Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val		270
	275	280
Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala		285
290	295	300
Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp		305
	310	315
Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr		320
	325	330
Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val		335
	340	345
Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg		350
	355	360
Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala		365
	370	375
Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu		380
385	390	395
Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala		400
	405	410
Val Ser Ala Cys		415
	420	

&lt;210&gt; 61

&lt;211&gt; 7

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Synthetic peptide inhibitor

&lt;221&gt; MOD\_RES

&lt;222&gt; 4

&lt;223&gt; Xaa = hydroxyethylene

&lt;400&gt; 61

Glu Val Met Xaa Ala Glu Phe

1

5

&lt;210&gt; 62

&lt;211&gt; 26

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 62

Leu Met Thr Ile Ala Tyr Val Met Ala Ala Ile Cys Ala Leu Phe Met



1                      5                      10                      15  
 Leu Pro Leu Cys Leu Met Val Cys Gln Trp  
                     20                      25

<210> 63  
 <211> 33  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <223> P26-P4'sw peptide substrate

<400> 63  
 Cys Gly Gly Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser Gly Leu  
 1                      5                      10                      15  
 Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Val Asn Leu Asp Ala Glu  
                     20                      25                      30  
 Phe

<210> 64  
 <211> 29  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <223> P26-P1' peptide substrate with CGG linker

<400> 64  
 Cys Gly Gly Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser Gly Leu  
 1                      5                      10                      15  
 Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Val Asn Leu  
                     20                      25

<210> 65  
 <211> 501  
 <212> PRT  
 <213> Mus musculus

<400> 65  
 Met Ala Pro Ala Leu His Trp Leu Leu Leu Trp Val Gly Ser Gly Met  
 1                      5                      10                      15  
 Leu Pro Ala Gln Gly Thr His Leu Gly Ile Arg Leu Pro Leu Arg Ser  
                     20                      25                      30  
 Gly Leu Ala Gly Pro Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp  
                     35                      40                      45  
 Glu Glu Ser Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val  
                     50                      55                      60  
 Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr  
 65                      70                      75                      80  
 Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser  
                     85                      90                      95  
 Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr  
                     100                      105                      110  
 Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val  
                     115                      120                      125  
 Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp  
                     130                      135                      140  
 Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile  
 145                      150                      155                      160  
 Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp

165 170 175  
 Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp  
 180 185 190  
 Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Ile Pro  
 195 200 205  
 Asn Ile Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln  
 210 215 220  
 Thr Glu Ala Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile  
 225 230 235 240  
 Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg  
 245 250 255  
 Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln  
 260 265 270  
 Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val  
 275 280 285  
 Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala  
 290 295 300  
 Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp  
 305 310 315 320  
 Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr  
 325 330 335  
 Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val  
 340 345 350  
 Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg  
 355 360 365  
 Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala  
 370 375 380  
 Val Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu  
 385 390 395 400  
 Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala  
 405 410 415  
 Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu  
 420 425 430  
 Gly Pro Phe Val Thr Ala Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro  
 435 440 445  
 Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala  
 450 455 460  
 Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp  
 465 470 475 480  
 Arg Cys Leu Arg Cys Leu Arg His Gln His Asp Asp Phe Gly Asp Asp  
 485 490 495  
 Ile Ser Leu Leu Lys  
 500

&lt;210&gt; 66

&lt;211&gt; 480

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 66

Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser Gly Leu Gly Gly Ala  
 1 5 10 15  
 Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp Glu Glu Pro Glu Glu  
 20 25 30  
 Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly  
 35 40 45  
 Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro  
 50 55 60  
 Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val  
 65 70 75 80  
 Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu

<400> 67  
Gly Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln  
1 5 10 15  
Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn  
20 25 30

Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro  
 35 40 45  
 His Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr  
 50 55 60  
 Arg Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp  
 65 70 75 80  
 Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn  
 85 90 95  
 Val Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe  
 100 105 110  
 Phe Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala  
 115 120 125  
 Glu Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu  
 130 135 140  
 Val Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly  
 145 150 155 160  
 Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly  
 165 170 175  
 Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu  
 180 185 190  
 Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val  
 195 200 205  
 Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr  
 210 215 220  
 Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu  
 225 230 235 240  
 Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser  
 245 250 255  
 Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val  
 260 265 270  
 Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser  
 275 280 285  
 Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile  
 290 295 300  
 Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln  
 305 310 315 320  
 Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val  
 325 330 335  
 Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala  
 340 345 350  
 Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu  
 355 360 365  
 Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu  
 370 375 380  
 Asp Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu Ser Thr Leu Met Thr  
 385 390 395 400  
 Ile Ala Tyr Val Met Ala Ala Ile Cys Ala Leu Phe Met Leu Pro Leu  
 405 410 415  
 Cys Leu Met Val Cys Gln Trp Arg Cys Leu Arg Cys Leu Arg Gln Gln  
 420 425 430  
 His Asp Asp Phe Ala Asp Asp Ile Ser Leu Leu Lys  
 435 440

&lt;210&gt; 68

&lt;211&gt; 395

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 68

Gly Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln  
 1 5 10 15

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Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn  
 20 25 30  
 Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro  
 35 40 45  
 His Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr  
 50 55 60  
 Arg Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp  
 65 70 75 80  
 Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn  
 85 90 95  
 Val Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe  
 100 105 110  
 Phe Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala  
 115 120 125  
 Glu Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu  
 130 135 140  
 Val Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly  
 145 150 155 160  
 Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly  
 165 170 175  
 Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu  
 180 185 190  
 Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val  
 195 200 205  
 Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr  
 210 215 220  
 Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu  
 225 230 235 240  
 Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser  
 245 250 255  
 Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val  
 260 265 270  
 Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser  
 275 280 285  
 Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile  
 290 295 300  
 Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln  
 305 310 315 320  
 Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val  
 325 330 335  
 Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala  
 340 345 350  
 Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu  
 355 360 365  
 Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu  
 370 375 380  
 Asp Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu  
 385 390 395

&lt;210&gt; 69

&lt;211&gt; 439

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 69

Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu  
 1 5 10 15  
 Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr  
 20 25 30  
 Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His  
 35 40 45

09724531.074701

Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys  
 50 55 60  
 Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly  
 65 70 75 80  
 Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala  
 85 90 95  
 Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser  
 100 105 110  
 Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro  
 115 120 125  
 Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His  
 130 135 140  
 Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu  
 145 150 155 160  
 Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly  
 165 170 175  
 Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile  
 180 185 190  
 Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn  
 195 200 205  
 Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser  
 210 215 220  
 Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe  
 225 230 235 240  
 Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe  
 245 250 255  
 Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly  
 260 265 270  
 Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly  
 275 280 285  
 Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr  
 290 295 300  
 Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys  
 305 310 315 320  
 Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile  
 325 330 335  
 Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly  
 340 345 350  
 Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala  
 355 360 365  
 Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn  
 370 375 380  
 Ile Pro Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met  
 385 390 395 400  
 Ala Ala Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys  
 405 410 415  
 Gln Trp Arg Cys Leu Arg Cys Leu Arg Gln Gln His Asp Asp Phe Ala  
 420 425 430  
 Asp Asp Ile Ser Leu Leu Lys  
 435

&lt;210&gt; 70

&lt;211&gt; 390

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 70

Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu  
 1 5 10 15  
 Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr  
 20 25 30

Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His  
 35 40 45  
 Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys  
 50 55 60  
 Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly  
 65 70 75 80  
 Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala  
 85 90 95  
 Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser  
 100 105 110  
 Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro  
 115 120 125  
 Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His  
 130 135 140  
 Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu  
 145 150 155 160  
 Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly  
 165 170 175  
 Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile  
 180 185 190  
 Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn  
 195 200 205  
 Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser  
 210 215 220  
 Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe  
 225 230 235 240  
 Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe  
 245 250 255  
 Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly  
 260 265 270  
 Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly  
 275 280 285  
 Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr  
 290 295 300  
 Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys  
 305 310 315 320  
 Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile  
 325 330 335  
 Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly  
 340 345 350  
 Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala  
 355 360 365  
 Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn  
 370 375 380  
 Ile Pro Gln Thr Asp Glu  
 385 390

<210> 71

<211> 374

<212> PRT

<213> Homo sapiens

<400> 71

Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val  
 1 5 10 15  
 Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val  
 20 25 30  
 Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp  
 35 40 45  
 Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu  
 50 55 60

His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg  
 65 70 75 80  
 Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu  
 85 90 95  
 Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg  
 100 105 110  
 Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly  
 115 120 125  
 Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg  
 130 135 140  
 Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr  
 145 150 155 160  
 His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro  
 165 170 175  
 Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile  
 180 185 190  
 Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro  
 195 200 205  
 Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile  
 210 215 220  
 Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys  
 225 230 235 240  
 Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val  
 245 250 255  
 Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys  
 260 265 270  
 Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala  
 275 280 285  
 Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met  
 290 295 300  
 Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln  
 305 310 315 320  
 Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr  
 325 330 335  
 Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val  
 340 345 350  
 Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile  
 355 360 365  
 Gly Phe Ala Val Ser Ala  
 370

<210> 72

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> P10-P4'staD-V peptide inhibitor

<221> MOD\_RES

<222> 10

<223> Xaa is statine moiety

<400> 72

Lys Thr Glu Glu Ile Ser Glu Val Asn Xaa Val Ala Glu Phe  
 1 5 10

<210> 73

<211> 9

<212> PRT

<213> Artificial Sequence



Thr 1	Gln	His	Gly	Ile 5	Arg	Leu	Pro	Leu	Arg 10	Ser	Gly	Leu	Gly	Gly 15	Ala
Pro	Leu	Gly	Leu	Arg	Leu	Pro	Arg	Glu	Thr	Asp	Glu	Glu	Pro	Glu	Glu
			20					25					30		
Pro	Gly	Arg	Arg	Gly	Ser	Phe	Val	Glu	Met	Val	Asp	Asn	Leu	Arg	Gly
		35					40					45			
Lys	Ser	Gly	Gln	Gly	Tyr	Tyr	Val	Glu	Met	Thr	Val	Gly	Ser	Pro	Pro
	50					55					60				
Gln	Thr	Leu	Asn	Ile	Leu	Val	Asp	Thr	Gly	Ser	Ser	Asn	Phe	Ala	Val
65					70					75					80
Gly	Ala	Ala	Pro	His	Pro	Phe	Leu	His	Arg	Tyr	Tyr	Gln	Arg	Gln	Leu
				85					90					95	
Ser	Ser	Thr	Tyr	Arg	Asp	Leu	Arg	Lys	Gly	Val	Tyr	Val	Pro	Tyr	Thr
			100					105					110		
Gln	Gly	Lys	Trp	Glu	Gly	Glu	Leu	Gly	Thr	Asp	Leu	Val	Ser	Ile	Pro
		115					120					125			
His	Gly	Pro	Asn	Val	Thr	Val	Arg	Ala	Asn	Ile	Ala	Ala	Ile	Thr	Glu
	130					135					140				
Ser	Asp	Lys	Phe	Phe	Ile	Asn	Gly	Ser	Asn	Trp	Glu	Gly	Ile	Leu	Gly
145					150					155					160
Leu	Ala	Tyr	Ala	Glu	Ile	Ala	Arg	Pro	Asp	Asp	Ser	Leu	Glu	Pro	Phe
				165					170					175	
Phe	Asp	Ser	Leu	Val	Lys	Gln	Thr	His	Val	Pro	Asn	Leu	Phe	Ser	Leu
			180					185					190		
Gln	Leu	Cys	Gly	Ala	Gly	Phe	Pro	Leu	Asn	Gln	Ser	Glu	Val	Leu	Ala
		195					200					205			
Ser	Val	Gly	Gly	Ser	Met	Ile	Ile	Gly	Gly	Ile	Asp	His	Ser	Leu	Tyr
	210					215					220				
Thr	Gly	Ser	Leu	Trp	Tyr	Thr	Pro	Ile	Arg	Arg	Glu	Trp	Tyr	Tyr	Glu
225					230					235					240
Val	Ile	Ile	Val	Arg	Val	Glu	Ile	Asn	Gly	Gln	Asp	Leu	Lys	Met	Asp
				245					250					255	
Cys	Lys	Glu	Tyr	Asn	Tyr	Asp	Lys	Ser	Ile	Val	Asp	Ser	Gly	Thr	Thr
		260						265					270		
Asn	Leu	Arg	Leu	Pro	Lys	Lys	Val	Phe	Glu	Ala	Ala	Val	Lys	Ser	Ile
		275					280					285			
Lys	Ala	Ala	Ser	Ser	Thr	Glu	Lys	Phe	Pro	Asp	Gly	Phe	Trp	Leu	Gly
	290					295					300				
Glu	Gln	Leu	Val	Cys	Trp	Gln	Ala	Gly	Thr	Thr	Pro	Trp	Asn	Ile	Phe
305				310						315					320
Pro	Val	Ile	Ser	Leu	Tyr	Leu	Met	Gly	Glu	Val	Thr	Asn	Gln	Ser	Phe
				325					330					335	
Arg	Ile	Thr	Ile	Leu	Pro	Gln	Gln	Tyr	Leu	Arg	Pro	Val	Glu	Asp	Val

			340					345				350			
Ala	Thr	Ser	Gln	Asp	Asp	Cys	Tyr	Lys	Phe	Ala	Ile	Ser	Gln	Ser	Ser
		355					360					365			
Thr	Gly	Thr	Val	Met	Gly	Ala	Val	Ile	Met	Glu	Gly	Phe	Tyr	Val	Val
	370					375					380				
Phe	Asp	Arg	Ala	Arg	Lys	Arg	Ile	Gly	Phe	Ala	Val	Ser	Ala	Cys	His
385					390					395					400
Val	His	Asp	Glu	Phe	Arg	Thr	Ala	Ala	Val	Glu	Gly	Pro	Phe	Val	Thr
			405						410					415	
Leu	Asp	Met	Glu	Asp	Cys	Gly	Tyr	Asn	Ile	Pro	Gln	Thr	Asp	Glu	
			420					425					430		

<210> 75  
 <211> 361  
 <212> PRT  
 <213> Homo sapiens

<400> 75

Met	Val	Asp	Asn	Leu	Arg	Gly	Lys	Ser	Gly	Gln	Gly	Tyr	Tyr	Val	Glu
1			5						10					15	
Met	Thr	Val	Gly	Ser	Pro	Pro	Gln	Thr	Leu	Asn	Ile	Leu	Val	Asp	Thr
		20					25						30		
Gly	Ser	Ser	Asn	Phe	Ala	Val	Gly	Ala	Ala	Pro	His	Pro	Phe	Leu	His
	35						40					45			
Arg	Tyr	Tyr	Gln	Arg	Gln	Leu	Ser	Ser	Thr	Tyr	Arg	Asp	Leu	Arg	Lys
50						55				60					
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